**PATENT** 

**ATTORNEY DOCKET NO.: 048283-0144** 

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(b) the hormone has a point mutation at amino acid 26 changing the amino acid from lysine (K26) to glutamine (Q26).

Please add the following new claims.

- --36. The composition of claim 31, wherein the composition has a hPTH (1-84) purity of at least 80%.
- 37. The composition of claim 36, wherein the hPTH (1-84) is nearly homogeneous.
- 38. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:
  - (a) providing a microorganism comprising:
    - (1) a leader sequence corresponding to the DNA sequence encoding Saccharomyces mating factor α1 lacking the yeast STE13 recognition; and
    - (2) a DNA sequence encoding hPTH, wherein the leader sequence and the hPTH sequence are operably linked;
  - (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
  - (c) purifying the resultant hPTH (1-84) protein.
- 39. The composition of claim 38, wherein the microorganism is selected from the group consisting of *Escherichia coli* and yeast.
- 40. The composition of claim 38, wherein the hPTH protein has a purity of greater than 90%.
- 41. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:

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- (a) providing a microorganism comprising:
  - (1) the first nineteen amino acids of the DNA sequence encoding Saccharomyces mating factor  $\alpha 1$  as a leader sequence; and
  - (2) a DNA sequence encoding hPTH, wherein the leader sequence and the hPTH sequence are operably linked;
- (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
- (c) purifying the resultant hPTH (1-84) protein.
- 42. The composition of claim 41, wherein the microorganism is selected from the group consisting of *Escherichia coli* and yeast.
- 43. The composition of claim 41, wherein the protein has a purity of greater than 90%.
- 44. A composition comprising recombinant human parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:
  - (a) providing a microorganism comprising:
    - (1) a leader sequence; and
    - (2) a DNA sequence encoding a derivative of hPTH, wherein the cleavage site after the pair of basic amino acids at positions 25 and 26 of the derivative hPTH gene has been modified such that the hormone is excluded as a substrate for yscF protease, wherein the leader sequence and the hPTH sequence are operably linked;
  - (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
  - (c) purifying the resultant hPTH (1-84) protein.
- 45. The composition of claim 44, wherein amino acid 26 of the human hPTH gene is modified from lysine to glutamine.

- 46. The composition of claim 44, wherein the leader sequence is the DNA sequence encoding *Saccharomyces* mating factor  $\alpha$ 1.
- 47. The composition of claim 44, wherein the protein has a purity of greater than 90%.
- 48. A composition comprising recombinant parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:
  - (a) providing a microorganism comprising:
    - (1) a leader sequence; and
    - (2) a DNA sequence encoding hPTH comprising an optimized consensus signal sequence having the following:
      - (i) a positively charged amino-terminal;
      - (ii) a hydrophobic core region; and
      - (iii) a polar COOH-terminal region,

wherein the leader sequence and the hPTH sequence are operably linked;

- (b) culturing said microorganism to allow expression of said DNA sequence encoding hPTH, thereby producing hPTH (1-84); and
- (c) purifying the resultant hPTH (1-84) protein.
- 49. The composition of claim 48, wherein the signal sequence is encoded by an amino acid sequence selected from the group consisting of: (1) Met-Lys-Ala-Lys-Leu-Leu-Val-Leu-Leu-Thr-Ala-Phe-Val-Ala-Thr-Asp-Ala; (2) Met-Arg-Ser-Leu-Leu-Ile-Leu-Val-Leu-Cys-Phe-Leu-Pro-Leu-Ala-Ala-Leu-Gly; and (3) Met-Arg-Phe-Pro-Ser-Ile-Phe-Thr-Ala-Val-Leu-Phe-Ala-Ala-Ser-Ser-Ala-Leu-Ala.
- 50. A composition comprising recombinant parathyroid hormone (hPTH) (1-84), wherein the hPTH is made by a process comprising the steps of:
  - (a) providing a microorganism comprising: